OMB INFORMATION COLLECTION
SUPPORTING STATEMENT

Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/Ps)
FINAL RULE
0910-0543

JUSTIFICATION

1. Circumstances Which Make this Information Collection Necessary

The Food and Drug Administration (FDA) is requesting Office of Management and Budget (OMB) approval of the information collection requirements in the final rule (Attachment A). The information collection requirements in 21 CFR Part 1271 are:

1271.3(n)	Reporting	Requires a documented dialogue about the donor's medical history and relevant social behavior, which would increase the donor's relevant communicable disease risk.
1271.47(a) and 1271.85(b)(2)	Recordkeeping	Requires the HCT/P establishment to establish and maintain procedures for all steps that are performed in determining eligibility, including the use of a product from a donor testing positive for CMV.
1271.47(d)	Recordkeeping	Requires the HCT/P establishment to record any deviation from the procedures.
1271.55(d)(4)	Recordkeeping	Requires the HCT/P establishment to retain records pertaining to HCT/Ps for 10 years.
1271.50(a)	Recordkeeping	Requires documentation of donor eligibility determination by a responsible person.
1271.55(a)	Reporting	Requires documentation of donor eligibility determination to accompany HCT/Ps.

1271.55(d)(1)	Recordkeeping	Requires the HCT/P establishment to maintain records of donor eligibility determination.
1271.55(d)(2)	Recordkeeping	Requires the HCT/P establishment to retain the original record and the statement of authenticity from the translator if any information on the donor is not in English.
1271.60(c)	Reporting	When an HCT/P is shipped in quarantine before completion of screening and testing, the donor identification, a statement that the donor's eligibility determination is not completed and that the HCT/P is not to be used until the determination is made, must accompany the HCT/P.
1271.60(d)(3) and 1271.65(b)(3)	Recordkeeping	When HCT/P from a donor whose eligibility determination is not complete is used in an urgent medical need, requires the HCT/P establishment to document notification of the physician that the testing and screening are not complete.

Because of their nature as derivatives of the human body, all HCT/Ps pose a potential risk of transmitting communicable diseases. For example, human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) have been detected in human tissue, including bone, skin, corneas, and semen. In proposing to establish a unified regulatory approach for HCT/Ps, the agency is responding to the concern about communicable disease transmission that is common to all such products.

FDA is promulgating these regulations solely under the authority of section 361 of the Public Health Service Act (PHS Act) (Attachment B). Under that section, FDA may make and enforce regulations necessary to prevent the introduction, transmission, or spread of communicable

diseases from one State or possession into any other State or possession, or from foreign countries into the States or possessions.

2. How, By Whom, and the Purpose for Collecting This Information

FDA is taking this action to provide more appropriate oversight for the wide spectrum of HCT/Ps that are marketed now or may be marketed in the future. FDA's action would improve protection of the public health and increase public confidence in new technologies, while permitting significant innovation and keeping regulatory burden at a minimum.

Documentation of donor eligibility determination provides to the user that all of the donor's medical history and social behavior were reviewed for high risk for or clinical evidence of communicable diseases, and that all of the required testing was completed. Each distributed HCT/P must have the following accompanying documentation: a distinct identification code; a statement, based on the screening and testing results, that the donor is determined to be eligible or ineligible; and a summary of the records used to determine eligibility. The summary of records must contain a statement that the testing was performed by a CLIA certified laboratory or by a laboratory that has met equivalent requirements as determined by the Centers for Medicare and Medicaid Services; a listing and interpretation of the results of all communicable disease tests performed; the name and address of the establishment determining the eligibility of the donor; and, in the case of an HCT/P from a donor determined to be ineligible based on screening and released for use under § 1271.65(b), a statement noting the reason for the ineligible determination.

Other reporting and recordkeeping requirements in 21 CFR part 1271 are designed to fully disclose the screening and testing results to the user when using products from donors who are determined to be ineligible or whose eligibility has not yet been determined in an urgent medical need. The distributing establishment is also to document that the HCT/P establishment notified the physician that the screening and testing are not completed.

HCT/P establishments are required to maintain records for a minimum of 10 years. Certain HCT/Ps have long storage periods and advances in medical diagnosis and therapy also have created opportunities for disease prevention or treatment many years after a recipient's exposure to a donor later determined to be at risk for communicable disease agents or diseases.

3. Use of Information Technology to Reduce Burden on the Public

Advanced methods of recordkeeping, (e.g., by an electronic method, have improved the ability of HCT/P establishments to more easily maintain and retrieve records of donor eligibility determinations. FDA is not aware of any other improved technology to reduce the burden.

4. Identification and Use of Duplicate Information

The agency has carefully created this regulatory framework for HCT/Ps that are not currently regulated by the agency to avoid unnecessary duplication of information collection. To avoid duplication, FDA is issuing technical amendments to 21 CFR parts 210, 211, and 820. These amendments state that in the event of a conflict between applicable regulations in parts 210, 211, and 820 and the regulations in part 1271, the regulation specifically applicable to the product in

question must supersede the more general.

5. FDA's Efforts to Reduce Burden on Small Business

Although FDA must apply the statutory and regulatory requirements equally to all enterprises, the agency does provide special help to small businesses. CBER's Office of Communication, Training and Manufacturers Assistance, provides assistance to small businesses subject to FDA's regulatory requirements.

6. Impact of Not Collecting This Information or Collecting Information Less Frequently

Less frequent collection of information or other methods of reducing the frequency of information would not provide the information needed to prevent the transmission of communicable diseases by HCT/Ps. The documentation of donor eligibility, the summary of records, and the information provided to physicians on the donor's eligibility when a product is used in an urgent medical need is the minimum necessary to keep the industry informed of the eligibility of each and every donor of HCT/Ps.

There are no technical or legal obstacles to reducing the burden.

7. Special Circumstances That Occur When Collecting This Information

The reporting burden under 21 CFR Part 1271, subpart C requires respondents to provide information more often than quarterly, i.e., for each individual HCT/P. This information includes an identification code number, which protects patient/donor confidential information.

8. Identification of Outside FDA Sources

As required by section 3506(c)(2)(B) of the Paperwork Reduction Act of 1995 (PRA), FDA provided an opportunity for public comment on the information collection requirements of the proposed rule (64 FR 52696 at 52715, September 30, 1999). Under the PRA, OMB reserved approval of the information collection burden in the proposed rule stating they will make an assessment in light of public comments received on the proposed rule. One letter of comment on the information collection requirements was submitted to the docket.

The comment stated that, although FDA invites comments on whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility, there are no data supporting any practical utility of the information collection, and that the estimated burden of the proposed collection of information is extremely low compared to the actual cost.

The reporting and recordkeeping information collection burdens are necessary to help ensure that the objective of the regulations, i.e., to prevent the transmission of communicable disease, is

fulfilled. These burdens allow FDA to monitor the compliance of HCT/P establishments with the regulations, which provide information to the consignee or user of the product that the donor of the product was adequately and appropriately screened and tested for evidence of specific disease agents.

The data in the proposed rule is not for the purpose of supporting the practical utility of the information collection, but for demonstrating how the burden is calculated. Although the comment states that the calculated burden is low, the comment did not offer additional data in support of the comment.

9. Payment or Gifts Offered to Respondents

No payment or gift was provided to respondents.

10. Method of Ensuring Respondent Confidentiality

The confidentiality of information received by FDA under the final rule is consistent with the Freedom of Information Act and the agency's regulations under 21 CFR Part 20. HCT/P establishments screening and testing human donors of cells and tissues are not required to reveal any proprietary information or trade secrets to achieve compliance with the final rule.

11. Use of Sensitive Questions

Questions of a sensitive nature, such as high-risk behavior related to the transmission of human immunodeficiency virus (HIV) and hepatitis, and other matters that are commonly considered private must be asked by the HCT/P establishments as part of the donor medical history evaluation. The answers to these questions help determine the eligibility of a donor, e.g., whether the donor was exposed to a communicable disease by participating in certain activities that are known to transmit communicable diseases. Donors not meeting certain criteria would be determined ineligible to donate. This information is necessary to prevent the transmission of relevant communicable diseases and to protect the public health. Such information would remain confidential by assigning a distinct identification code to the donor instead of using a name. FDA may review such information during an inspection.

12. Burden Hours and Costs Associated With This Information Collection

The estimated annual reporting and recordkeeping burden for this information collection is 866,240 hours.

Based on updated information from FDA's registration data and trade organizations, FDA has estimated the following burden. When an estimate was not available for the annual frequency of

either responses or records, we divided the estimated total annual responses or records with the applicable number of respondents or recordkeepers. Total hours are calculated by multiplying

the total annual responses or records by the hours spent per response or record.

Estimated Annual Reporting Burden

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
1271.3(n)	1,302	60	78,136	1.0	78,136.0
1271.55(a)	1,235	787	972,417	0.5	486,208.5
1271.60(c)	1,069	208	222,417	0.5	111,208.5
Total					675,553.0

Estimated Annual Recordkeeping Burden

21 CFR Section	No. of Recordkeepers	Annual Frequency per Recordkeeping	Total Annual Records	Hours per Record	Total Hours
One-time Burden (Creation of SOPs) 1271.47(a) and 1271.85 (b)(2)	510	5	2,550	16	40,800
One-time Burden (Review of existing SOPs for compliance)	792	5	3,960	8	31,680
SOP Update	1,302	5	6,510	2	13,020
1271.47(d)	1,102	1	1,102	1	1,102
1271.55(d)(4)	195	1	195	120	23,400
1271.50(a)	510	9	4,640	5	23,200
1271.55(d)(1)	329	162.85	53,579	1	53,579
1271.55(d)(2)	1,302	1	1,302	1	1,302
1271.60(d)(3) and 1271.65(b)(3)	1,302	1	1,302	2	2,604
Total					190,687

In estimating the burden, we compared the regulations with the current voluntary standards of a number of industry organizations, such as, the American Association of Tissue Banks, Eye Bank Association of America, American Association of Blood Banks, Foundation for the Accreditation of Cellular Therapy, National Marrow Donor Program, and College of American Pathologists, and the guidelines provided by American Society of Reproductive Medicine. In those cases where a voluntary industry standard appears to be equivalent to a regulation, we assumed that any reporting or recordkeeping burden is a customary and usual business practice of HCT/P establishments who are members of those organizations and no additional burden is calculated here.

Under § 1271.3(n), approximately 1,302 establishments (300 conventional and eye tissue establishments, 425 peripheral and cord blood stem cell establishments, 510 reproductive tissue establishments, and 67 manufacturers of products regulated under the Federal Food, Drug, and Cosmetics Act and section 351 of the PHS Act) are required to have a documented medical history interview about the donor's medical history and relevant social behavior as part of the donor's relevant medical records for each of the estimated 78,136 donors (approximately 20,000 conventional tissue donors, 47,796 eye tissue donors, 5,700 peripheral and cord blood stem cell donors, and 4,640 reproductive cell and tissue donors). We estimate that the time to conduct the interview with the donor, if living, or with an individual able to provide the information sought in the interview is one hour.

Under § 1271.55(a), 972,417 HCT/Ps (approximately 750,000 conventional tissues, 94,186 eye tissues, 6,031 stem cells, and 122,200 reproductive cells and tissues) are distributed per year. The agency estimates that for each HCT/P, 1,235 establishments will expend approximately 0.5 hours to prepare the summary of records. Conventional and eye tissue establishment are currently required to provide a summary of records under § 1270.33(d), which § 1271.55 replaces.

Under § 1271.60(c), a record consisting of donor identification and a statement that the donor-eligibility determination is not completed and that the HCT/P is not to be used until the determination is completed, must accompany each HCT/P shipped under quarantine. We estimate that approximately 1,069 establishments may ship an estimated 222,417 HCT/P under quarantine and that the preparation of the record would take approximately 0.5 hours.

We assume that approximately 510 reproductive HCT/P establishments would create 5 SOPs under §§ 1271.47(a) and 1271.85(b)(2) for a total of 2,550 records, and we estimate that it would take 16 hours per new SOP for a total of 40,800 hours as a one-time burden. We estimate that up to 5 SOPs would already exist for 792 HCT/P establishments as a result of complying with current applicable regulations or following industry organizational standards, and that it would take each establishment approximately 8 hours per SOP to complete the review for compliance with the requirements for a total of 31,600 hours as a one-time burden.

Once the SOPs are created, annual SOP maintenance of existing SOPs is estimated to involve 2

hours annually per SOP for all HCT/P establishments. Annual total hours for maintaining the SOPs is estimated at 13,020.

Under § 1271.47(d), an estimated 1,102 HCT/P establishments would take approximately one hour to annually document one deviation from an SOP.

Under § 1271.55(d)(4), we estimate that 195 HCT/P establishments not currently following existing industry standards will expend 120 hours (10 hours per month) annually to maintain records for 10 years.

Under § 1271.50(a), documentation of donor eligibility is required for the first time for approximately 510 reproductive tissue establishments. Out of a total of 1,302 establishments of HCT/Ps, there would be no added burden for approximately 792 other establishments who document donor eligibility as usual and customary business practice under the trade organization standards. FDA estimates that § 1271.50(a) would impose a new collection of information requirement on 510 establishments of reproductive HCT/Ps, each of which would document the eligibility of an estimated 9 donors per year, or 4,640 donors, expending approximately 5 hours per document.

Approximately 329 HCT/P establishments would maintain screening and testing records under § 1271.55(d)(1) for an estimated 53,579 donors, which would take approximately one hour per donor.

For documents originally not in English, approximately 1,302 HCT/P establishments would maintain a record of translation with an authenticity statement by the translator and the original documents. We estimate that it would take one hour for each establishment to maintain one such document annually.

Under § 1271.60(d)(3) and 1271.65(b)(3), when an HCT/P that is unsuitable or not fully screened or tested is used, approximately 1,302 establishments of HCT/Ps are required to document the reason for using the product, and notice of the results of testing and screening to the physician. The agency estimates that such documentation would occur approximately once annually per establishments and that each establishment would expend approximately 2.0 hours to create such document.

Under section 1320.3(c)(2) of the PRA the labeling requirements in proposed § § 1271.60(d)(2), 1271.65(b)(2), 1271.65(c)(1) and (2), 1271.80(b)(1), (2), and (3) do not constitute collection of information because information required to be on the labeling is originally supplied by FDA to the establishments for the purpose of disclosure to the public to help ensure a safe supply of HCT/Ps and protect public health.

The reporting of screening and testing results to the physician in § 1271.60(d)(4) does not

constitute collection of information burden because it is calculated under the requirement for § 1271.55(a).

In the supporting statement submitted for the proposed rule, we included the information collection burden for registration and listing requirements under §§ 207.20, 807.20, and 1271.10. These requirements are currently approved under OMB number 0910-0469 and, therefore, are not included in this estimate.

In the proposed rule, we underestimated the number of respondents. Based on updated information from FDA's registration data and trade organizations, we have revised our estimate of establishments to approximately 1,302.

We also have adjusted our estimates for the number of HCT/Ps annually produced based on updated information from industry provided to us at the time we prepared the final rule.

Our burden estimates for the annual frequency per response and average hours per response are based on institutional experience with comparable reporting and recordkeeping provisions for biological products. Also, we are adding a reporting burden estimate for § 1271.3(n) and a recordkeeping burden estimate for § 1271.47 that were not included in the proposed rule.

13. Annual Cost Estimate to Respondents

There are no capital and start-up, and operation maintenance and purchase costs associated with the collection of information requirements.

Costs to Respondents

Activity	No. Of Hours	Cost per Hour	Total Cost
Reporting	675,553	$28	$18,915,484
Recordkeeping	85,500/105,187	$40/$28	$6,365,236
Total			$25,280,720

The annual cost to respondents is estimated at $25,280,720 based on the following information. An establishment's supervisor at $40/hour will expend approximately 85,500 hours to create, review, or update SOPs. A medical technician, at an hourly wage of $28.00/hour, would be responsible for the other reporting and recordkeeping requirements [190,687 - 85,500 = 105,187] [105,187 + 675,553]. The salary estimate includes benefits but no overhead cost.

14. Annual Cost Estimate to FDA

The total estimated annual cost to the Federal Government is $1,304,746.90. This figure is based on the costs for inspections of establishments. (The cost for registration start-up and operation

are described in OMB # 0910-0469.)

There are approximately 725 establishments (300 conventional HCT/P establishments and 425 peripheral and cord blood stem cell establishments) that would be inspected on a biennial basis. Therefore, it is estimated that approximately half (362 establishments) would be inspected annually at an estimated annualized cost to the Federal Government of $1,200,942.20. This estimate is based on approximately 69 hours for each inspection performed by an FTE at a pay rate of $48.08 per hour (average FTE salary of $100,000 from the ORA work plan model). This cost includes inspection of an establishment, review of its records and the establishment inspection report write-up.

There are approximately 510 reproductive HCT/P establishments that would be inspected for compliance with the donor eligibility requirements every 4 years. Therefore, it is estimated that approximately one-fourth (127 establishments) would be inspected annually at an estimated annualized cost to the Federal Government of $103,804.72. This estimate is based on approximately 17 hours for each inspection.

Inspections are already occurring for the 67 manufacturers of HCT/Ps regulated under the act and section 351 of the PHS Act.

15. Changes from Previous Approval

Changes in burden are not applicable as this is the first submission of the final rule and is a new collection.

16. Publishing the Results of This Information Collection

There are no tabulated results to publish for this information collection.

17. Reason for Not Displaying the OMB Approval Date

FDA is not seeking approval to exempt the display of the expiration date of the OMB approval.

18. Explanations to Section 19, "Certification for Paperwork Reduction Act Submissions"

There are no exceptions to Item 19 of OMB Form 83-I.